Fat Embolism, ARDS, Coma, Death: The Four Horsemen of the Fractured Hip

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Abstract

The pathophysiology of fat embolism syndrome (FES) is presented in the context of total joint arthroplasty. The current literature is reviewed with recommendations for surgical technique, anesthetic and pulmonary management. Diagnosis is quite difficult but can be established by imaging techniques such as MRI, SPECT, and transcranial Doppler sonography. Early steroid treatment may limit morbidity.

Total joint arthroplasty has become one of the most common orthopedic procedures in the elderly. Approximately 3.8% of the U.S. population have significant osteoarthritis and an estimated 20% will eventually require hip or knee replacement.[1] The complication rate from all causes is about 2%, while mortality in the perioperative period is about 0.1%.[2] One of the most serious and potentially lethal complications of hip replacement is the fat embolism syndrome (FES). Patients who are also at risk for FES are those with multi-trauma injuries, especially with long bone fractures, and those with pathologic fractures from tumors. When these numbers are combined with elective joint procedures in the elderly, it is estimated that as many as 5000 deaths are caused annually by this complication.[3] We report two cases of FES at our institution and review the recent literature concerning recommendations for orthopedic, anesthetic and pulmonary management.

Case 1. An 88-year-old man presented with a left hip fracture after a fall in his retirement home. He denied dizziness or loss of consciousness. Past history was significant for atherosclerotic heart disease including hypertension, previous MI, bypass graft surgery in 1983, and a pacemaker. He also had a long history of chronic obstructive lung disease and dyspnea following minimal exertion. Other history included peripheral neuropathy, previous trans-urethral resection of the prostate for cancer, and glaucoma with recent detached retina. Medications included terazosin, digoxin, tobramycin eye drops and ipratropium and albuterol inhalers. Physical examination was unremarkable except for his hip fracture; lungs were clear and heart sounds normal without murmur or gallop. There was no peripheral edema, organomegaly, or venous distension suggestive of congestive heart failure. He was brought to the operating room for a bipolar hemi-arthroplasty utilizing a Biomet system. Monitoring included automated BP, EKG, pulse oximetry, end tidal CO2, esophageal stethoscope and temperature, and indwelling urinary catheter. General anesthesia was induced with thiopental, fentanyl, isoflurane, and intubation was facilitated with succinylcholine. Muscle relaxation was continued with cis-atracurium. The operative course was smooth until the time of the insertion of the prosthesis. The medullary canal had been reamed with a rigid manual reamer and a 25 mm cement restrictor had been placed distally. The canal was thoroughly irrigated with pulsatile irrigation, and two units (80 grams) of methylmethacrylate cement were placed with an injection gun for pressurization. The prosthetic stem was then inserted into the cement and tapped into position. Approximately ten minutes later Sp02 fell from 98 to 81%, and two minutes after that BP fell from 130/80 to 80/50 mm HG. Ephedrine bolus of 20, then 30 mg had little effect and BP declined further to 60/30 mm Hg. Bolus doses of epinephrine brought pressures back to 140/90 range, but 02 sat remained low at 81-85%. The patient was turned and wound closure was completed in the supine position. Radial artery and pulmonary artery catheters were placed, and norepinephrine infusion was utilized to support BP and cardiac output. Post operative chest film showed bilateral fluffy infiltrates consistent with pulmonary edema. Pressor infusion was changed to dobutamine and furosemide was given. EKG showed a paced rhythm and nonspecific ST- T wave changes. Despite bronchodilators, PEEP ventilation, and inotropic support the patient's condition continued to deteriorate and he expired 2 hours later. No post mortem exam was performed.

Case 2. A 70-year-old man slipped on beach access stairs and sustained a hip fracture. Past history was unremarkable except for a long-standing seizure disorder under treatment with phenytoin. He was admitted in the evening and put at bed rest with traction for the night. Physical exam was negative except for hip fracture; lungs were clear and cardiac exam was normal. The next morning he became febrile and 02 saturation by pulse oximetry was noted to be low. ABG on room air showed a p02 of 45, pCO2 38, pH 7.36, although breath sounds were still clear and there was no complaint of dyspnea. The patient was oriented and cooperative but became increasingly somnolent as the day progressed. He was brought to the OR for left hip arthroplasty on the evening 24 hours following admission. He received a general anesthetic induced with thiopental, fentanyl and midazolam, maintained with isoflurane inhalation and supplemented with a total of morphine 12 mg during the procedure. Reaming and cement injection were carried out as in case one. Approximately four minutes following insertion of the prosthesis stem, the BP transiently fell from 150/90 to 104/65 mm Hg and Sp02 from 98 to 93%. A low dose infusion of epinephrine was utilized for about 10 minutes until pressures returned to stable levels.

In the recovery room the patient awoke appropriately and was able

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to follow commands to deep breathe and move his extremities but was otherwise quite somnolent. His 02 saturation on 4 liters by nasal prongs stayed in the 95-98% range. He was transferred to the general floor with nasal 02. Three hours later his 02 sat again fell to 81-86% range, and his level of consciousness decreased. With higher 02 flows his 02 sat remained above 90% but respiratory effort was irregular and he became increasingly less responsive to stimulation, arms were held in flexed position with hands clenched.

Upon transfer to ICU his vital signs remained stable and 02 sats were kept above 95% with continuous positive pressure face mask. Chest X-ray showed mild pulmonary congestion and pulmonary capillary wedge pressure was slightly elevated at 19 mm Hg. A helical chest CT scan revealed only dependent atelectasis bilaterally and a small effusion but no evidence of segmental or subsegmental embolization.

The clinical picture was felt to be consistent with FES with acute respiratory distress syndrome. Petechiae were not seen, however, and urine when it was checked for fat at the end of surgery was negative.

Unfortunately the level of consciousness did not improve. Head CT was negative for infarction or bleeding and repeat 48 hours later was also normal. EEG showed diffuse slow waves consistent with minor epileptiform activity. The phenytoin level was initially found to be low but rose to therapeutic levels with higher dosage.

Post op blood counts were lower than expected from the 400 ml operative blood loss and may have been depressed by fat embolism. Admission Hgb and Hct were 12.2 and 35.8 and decreased to 7.7 and 22.2 respectively. Platelet count decreased from 172,000 to a low of 101,000.

The patient, still comatose and intubated, was transferred by air ambulance to a hospital near his home in California. He recovered very little function, and subsequent MRI was interpreted by his neurologist as consistent with fat embolism syndrome.

Discussion

Both of these cases demonstrate a sequence of events characteristic of FES and myocardial depression from methacrylate. Case number one had little cardiac and pulmonary reserve and a rapid downhill course. Case number two may have had FES from his initial fracture and a repeat insult during surgery. He also had cardiopulmonary depression at the time of cemented long-stem prosthesis but tolerated it reasonably well. His poor outcome may have been due to cerebral FES or post-op hypoxia from evolving pulmonary FES.

Pathophysiology

Fractures that disrupt the medullary cavity are at risk for causing leakage of fat and marrow contents into the general circulation. An unstable fracture site may allow movement of the fracture hematoma and allow marrow components to escape. Early surgical intervention is therefore theoretically advisable, and indeed has been shown to improve outcome.[4] Operative manipulation, and especially long-stem instrumentation with cement, may substantially increase the risk and severity of FES[5] and deserves further discussion below.

Presenting symptoms and signs of FES may be mild and may not even begin for as long as five days post injury. Most often, however, symptoms peak at 24-48 hours. The hallmark is arterial hypoxemia, often accompanied by fever, sinus tachycardia and altered mental status. Petecchiae, usually present over the anterior chest, axilla, and sclerae, develop in about half of patients and fat globules may be present in urine and blood samples. Plain chest X-ray is positive in only 1/3 to 1/2 of patients and then shows a fluffy infiltrate. Ventilation-perfusion scan and helical CT usually demonstrate patchy widespread embolic patterns. EKG may show right heart strain and ischemia.

The hemiarthroplasty surgical technique described in our two cases involves reaming of the femoral medullary shaft with a manual rasp cusped reamer. This procedure loosens the medullary contents, enlarges the cavity, and prepares the bone for introduction of a long-stem prosthesis. The methylmethacrylate cement is injected under pressure with a device similar to a caulking gun and a distal plug limits spread and ensures good penetration of the cement into the interstices of the bone. Mechanical extrusion of air, fat and medullary debris may occur with this maneuver and these elements can be "intravasated" into the blodstream. In a dog model, femoral shaft pressures in greyhounds rose as high as 900 mm Hg with gun injection.[6] In humans pressures up to 300 mm Hg have been measured.[7] Marrow contents and air have been suggested by Doppler ultrasound studies over the femoral veins,[8] and blood samples from PA and venous catheters confirm gross and microscopic particles of marrow, platelet and fibrin aggregates in humans.[9] The methacrylate monomer itself has been shown to be present in blood samples and may contribute to cardiac depression.[10]

Probst[11] studied 20 patients undergoing total hip arthroplasty with trans-esophageal echocardiography (TEE). All subjects demonstrated emboli in the heart. Some were small, consistent with microbubbles of air, and some larger patterns suggested solid material. Segmental wall motion abnormalities (SWMA) occurred in 14 of 20 patients, more commonly during insertion of cemented femoral components. The authors concluded that pulmonary embolism is a frequent occurrence, however most often it presents no clinically significant problem. SWMAs may occur secondary to either PE and/or methylmethacrylate depression.

Medullary fat and debris are swept into the venous bloodstream and reach the pulmonary circulation. Gas exchange is rapidly impaired and SpO2 by pulse oximetry falls precipitously.

Pulmonary arteriolar vasoconstriction raises pulmonary artery pressure and right heart strain ensues. The right heart has a low tolerance to hypertension and may suddenly fail, leading to pulmonary edema and cardiovascular collapse. To make matters worse, approximately 10-30% of patients has a flow patent foramen ovale. As right heart pressures increase and approach left sided pressures, the overlapping membranes of the atrial septum may "float" apart; the foramen ovale opens and allows direct paradoxical embolization into the left atrium. And here emboli cause real trouble. Air emboli into coronary ostia may cause electromechanical dissociation; particulate material may cause myocardial infarction. Emboli to the cerebral arteries may cause a focal stroke.

Fat intravascated into the venous circulation may not be completely filtered by the lungs. In the pulmonary capillaries, some air and fat may traverse the bed, or travel by pulmonary shunts into the systemic circulation. A recent study by transcranial Doppler has documented 8 of 20 subjects with evidence of embolic signals following impaction of a cemented femoral component.[12] The FES

syndrome may therefore extend from ARDS to cardiac and CNS complications as well.

Twelve hours to 3 days later, fat emboli trapped in the lung microvasculature cause more disruption that can be accounted for by simple mechanical obstruction. In response to the fat, the pulmonary parenchyma secretes lipase which hydrolyzes the non-toxic neutral fat into free fatty acids and glycerol.[13] These chemically toxic metabolites cause alveolar injury, increased capillary permeability, and damage to lung surfactant leading to ARDS.[14] A similar pathological response may take place in the cerebral cortex.[15]

The diagnosis of cerebral fat embolism can be difficult to make since the signs of CNS depression are nonspecific and may be due to embolism from clot, air or particulate matter. Hypoxia secondary to altered lung function, depression from pain medication or anesthetic drugs, or decreased cerebral function in a stressed elderly person (sundowner syndrome) may further cloud the issue.

Recently developed imaging techniques may help to establish the diagnosis: magnetic resonance imaging (MRI), transcranial Doppler sonography, and single photon emission computed tomography (SPECT).[16,17] The neurological dysfunction can be quite severe, as we report in Case 2, and may exceed the level of respiratory distress. The mechanism is not well understood. Two theories have been proposed to explain the brain injury: (1) the mechanical theory, in which fat globules obstruct flow in cerebral vessels, and (2) the toxic theory, in which toxic free fatty acids are released and induce endothelial damage and enhance vascular permeability.[18] Small lesions may produce transient perivascular edema with subsequent full recovery. Larger lesions may cause petechial hemorrhage and irreversible infarction.

Orthopedic Management

Patterson[19] and Ereth[20] have enumerated several considerations in surgical technique. The first concern is the choice of prosthesis used for implantation. If a long-stem femoral component is indicated, the tendency is toward the use of a non-cemented prosthesis. The length of the femoral stem should be minimized. Careful preparation of the femoral canal should first be carried out with rigorous irrigation and suctioning of clot, debris and medullary fat. Pressurization is a part of modern cement technique to improve implant/bone bonding and reduces the incidence of loosening and later need for revision, but over-pressurization must be avoided. Several modifications of technique have been suggested to avoid excessive pressures in the medullary canal: (1) elimination of the cement-restrictor plug in the distal shaft, (2) packing of cement rather than gun injection, (3) retrograde injection around a seated component, and (4) placement of a 0.6 cm (one-quarter-inch) venting hole distal to the femoral isthmus. Additional safeguards are overdrilling the size of the femoral shaft,[21] venting the femoral shaft with an evacuation catheter,[22] and utilization of a prosthesis design with a fluted stem.[23]

Once all precautions have been taken and the cement and long-stem prosthesis are put in place, the moment of truth arrives. It is then incumbent upon the anesthesiologist to monitor, detect, and treat complications should they arise.

Anesthetic Management

Prevention is the most desired endpoint if alterations to orthopedic technique are instituted to improve safety. From the numerous reports of cardiac arrest in the literature,[24,25,26,27,28,29,30,31,32,33,34] it is clear that the fully developed syndrome of pulmonary embolism when combined with methacrylate myocardial depression portends a catastrophic intraoperative event. This has been termed "the cement implantation syndrome."[35]

Table 1.— Implant Precautions (**after Patterson**)

- Non-cemented prosthesis
- Minimize length of stem
- If cement used, avoid over-pressurization of cement in medullary canal
  - -omit distal cement restrictor plug
  - -venting hole in bone
  - -overdrill size in medullary shaft
  - -venting catheter
  - -retrograde injection or "packing" of cement
  - -fluted long-stem component

Lesser manifestations, however, are likely to be commonly encountered and anesthetic techniques can be attuned to discover early warning signs and cope with the ensuing events.

Either spinal or general anesthesia is acceptable. Spinal has gained popularity in recent years for its numerous advantages: lowered blood loss, less post-op DVTs, hypotension attenuated by sympathectomy, and excellent intraoperative protection from the stress of surgical pain. However, if problems arise with oxygenation or breathing, intubation in the lateral position may be difficult.

Combining spinal or epidural with light general anesthesia offers the advantages of both techniques. Epidural may offer additional benefit of providing analgesia into the post-operative period with both local anesthetic agents and epidural narcotics. There is added risk, however, of injury to the spinal cord from hematoma if coagulation derangement is encountered. Also technical difficulties in moving patients with fractures and in placing catheters in elderly patients with arthritic spine changes and spinal stenosis must be weighed. Standard monitoring should include blood pressure cuff, EKG, pulse oximetry, end-tidal C02, esophageal stethoscope, temperature, and urinary bladder catheter.

Higher risk joint procedures include primary total hip for metastatic cancer or bone tumor, revision of a total hip, bilateral total knee, and primary total hip or knee with a cemented long-stem component.[36] These usually merit invasive monitoring with large bore central venous access and a radial artery catheter. Swan-Ganz catheters have well documented value but add risk of their own, such as pulmonary artery rupture and infection. Some authors use them routinely to monitor for PE and to assess risk for proceeding with a second total knee implant[37,38], others reserve them for specific cardiac indications. Trans-esophageal echo (TEE) is a newer noninvasive monitor which may provide early warning information with less risk.

Rescue drugs must of course be immediately at hand and drips must be pre-mixed and ready to infuse. Waters in a dog model found calcium and atropine the best drugs to reverse methylmethacrylate depression.[39] Patterson's group routinely begins low dose epinephrine infusion at the time of the placement of cement and prosthesis. Post-operative monitoring should include pulse oximetry for high risk cases to be alert for hypoxemia in early FES.

Table 2.— Techniques and Monitoring (**after Enneking**)		
Orthopedic techniques	Anesthesia techniques	Monitoring
Low Risk		
Percutaneous pins ORIF with compression screw and side plate Non-cemented prosthesis	Spinal or epidural or general anesthesia	Non-invasive BP, EKG, CO2, Sp02, temperature
High Risk		
Above with heart or pulmonary disease Presence of cancer or tumor Long-stem component with cement Bilateral total knee	General with/without epidural or spinal	Above plus arterial line and CVP Possible Swan-Ganz or TEE

Pulmonary Management

The pulmonary service is frequently consulted to optimize management of patients at risk of FES. The triad of hypoxia, fever, and mental changes warrants careful evaluation as no definitive laboratory or X-ray test exists for diagnosis.[40,41] To eliminate the more common sources of thrombotic PE, duplex scan of pelvic and lower extremity veins is often a first step. Plain chest films may be helpful but ventilation-perfusion scan or helical CT gives more information. Pulmonary angiography may be indicated in the presence of significant PE from thrombi, and inferior vena cava filters are sometimes a lifesaving intervention when pelvic clots are present.

A number of drugs have had their day in the treatment of FES: ethanol, heparin, low-molecular-weight dextran, and hypertonic glucose.[42] Only steroids however, have demonstrated an improvement in outcome. A prospective, double-blind randomized study of trauma patients at high risk for FES found a dose of methylprednisolone 7.5 mg/kg every 6 hours for 3 days to be effective in prevention of the syndrome.[43]

The mechanism, although still unproven, may be preservation of vascular integrity, stabilization of granulocytic lysosomal membranes, retarding of platelet aggregation, and minimizing the transudation of interstitial fluid.

Timing of surgery for a fractured hip is also an important consideration. In general terms, the axiom that the patient is most healthy and has the most physiologic reserve at the time he enters the ER still holds true. But in the real world in which we live, other considerations intervene: access to an operating suite, availability of a skilled surgeon and staff, the need for consultations from specialists, and time needed for studies all must be taken into account.[44] When considering early stabilization of a hip fracture, there also may well be a background of fat embolism and a nadir of pulmonary function for which the team must be ever alert. FES has an incidence in hip and knee surgery as high as 14%, and of those patients 10-20% may die or suffer significant neurological impairment.[45] For the survivors, FES is a self-resolving illness and the mainstay of treatment is respiratory support.[46]

Conclusion

FES occurs as a consequence of multi-trauma, long bone fracture, or total joint arthroplasty. Surgical technique has been modified to reduce the incidence, especially when long-stem cemented components are used. Anesthetic techniques are geared to early discovery and management of cardiac and pulmonary depression. Cerebral involvement is best diagnosed by MRI and SPECT. Early treatment with steroids can be considered in certain settings.

Commentary

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Fat embolism syndrome causing death, especially in the patient undergoing elective reconstructive surgery, is traumatic to all concerned: patient, family and surgeon. This review article appropriately considers both the orthopedic technical and the anesthesia factors involved in detecting and preventing FES in the acute fractured hip patient. In the case of an emergency the surgeon and anesthesiologist are limited to a certain extent in the preoperative evaluation and prophylactic treatment. This is especially true with elderly (frequently high medical risk) patients who do not improve their medical status by delaying surgery.

Elective reconstructive surgery of the hip and knee allows a time frame that can be utilized to decrease the risk of FES. The literature review and my personal observation confirm that a pre-operative compromised pulmonary function increases the risk of fatal FES. Controversy exists concerning the safety of doing simultaneous bilateral total knee replacements, with decreased cost, versus staged knee replacements. The data indicates increased risk of FES in simultaneous knee replacements. A thorough pulmonary evaluation, including functional testing, would help make the decision to proceed with simultaneous bilateral knee replacements.

Increased intramedullary pressure during instrumentation does introduce fat and other particulate matter into the venous system, to the lungs and often the brain. Using sharp fluted reamers, fluted intramedullary alignment rods and decreasing the pressure in the canal during the procedures should always be considered. However the surgeon should not sacrifice optimum technique in trying to decrease the risk of FES.

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